American Chemistry Council | Biocides Panel

June 23, 2017

Undocumented Expansion of Data Requirements

The ACC Biocides Panel (the Panel) is concerned that EPA is expanding the data requirements for antimicrobials in a number of ways. In some cases these extend data requirements beyond the recently codified under 40 CFR Part 158, Supbart W. In others, the basis for the request for "new" data is not apparent.

The Panel often learns of the new data requirements from a Panel member as that member engages with the Agency on a specific product or active ingredient registration or reregistration. In some of these situations, it appears that EPA is institutionalizing a new requirement but doing so without providing the registrant or the antimicrobial industry at-large a reason for the required data. The costs associated with responding to these demands from EPA can be significant; thus the ever increasing costs of registration and reregistration are stifling innovation and the industry's ability to bring products to market.

As explained below, the Panel believes that EPA is not fully committed to its objective of transparency and openness. In addition, these actions are contrary to good administrative practice and, in the Panel's view, to applicable legal requirements. The Panel urges EPA's commitment to a public process that includes stakeholder input before modifying the ways in which it views exposures and/or imposes new data requirements. We also ask EPA to carefully consider the examples below and, as appropriate, rectify the situation.

Example 1: Data to Support a Dietary Risk Assessment for Products with No Food Uses

In a number of Reregistration Eligibility Decisions (REDs), EPA has required additional long-term toxicity and other information to support a dietary risk assessment for products that have historically been considered not to have any food uses. Without such data, the RED informs registrants that an adverse decision on the nonfood uses was possible.

The following are examples:

1.1 RED for 2-((hydroxymethyl)-amino)ethanol (HHT/HMAE) (EPA Case No. 3070). Both the Human Health Effects Scoping Document and Registration Review Summary state that:[1]

> Dietary (food) exposure could potentially occur because HHT/HMAE is used as a process preservative and an in-can preservative for materials containing water as a major ingredient such as caulks, adhesives, sealants that may be used in food contact situations such as food preparation, food

[1] *See* Docket No. EPA-HQ-OPP-2008-0879 at [HYPERLINK "http://www.regulations.gov"] for the Registration Review case file; Human Health Effects Scoping Document at 8.

processing, and food serving areas. A dietary exposure and risk assessment has not been conducted in the past. However, migration of HHT/HMAE from these preserved materials to food may occur to some extent. Therefore, a dietary (food source) risk assessment is recommended during the risk assessment stage of Registration Review. However, certain chemistry, use pattern, and chronic/cancer studies are being recommended to permit more appropriate exposure estimates and the selection of an endpoint for use in a chronic dietary risk assessment. Note that FDA does not currently regulate HHT/HMAE as a direct or indirect food additive.

This new approach is based upon speculation and will make virtually every preservative use a "food use". As the Panel has indicated to EPA, changes such as this should be approached through some public process that provides an opportunity for dialog and input before any new requirements are imposed. In this situation, the registrant offered labeling to prevent its use in food contact applications, but EPA rejected this solution. Rejection of a labelling solution represents another serious issue. EPA should follow applicable legal requirements and good administrative practice by implementing such a change only after a public process.

1.2 The requirement for a dietary risk assessment for non-food uses has been advanced in several other registration review cases including Busan and Oxazolidine-E.[2] However, the requirement has not been applied consistently; for some registration review cases, even though chemistries are similar and use patterns are the same, a dietary risk assessment has not been required.[3] These inconsistencies create an uneven playing field among registrants and lead to a high level of unpredictability on the costs and time required to respond to EPA's registration reviews.

EPA has asserted that a dietary risk assessment is required in the registration review of Oxazolidine-E based on the use of the preservative in surfactants that may become components of dishwashing liquids and surface cleaners. The Agency acknowledges that these are not "direct or indirect food uses," (no approval under FFDCA section 408 or 409 is needed) but nonetheless EPA asserts that a "Tier 1 dietary screening level assessment" is triggered and that EPA "must conduct risk assessments to ensure that Oxazolidine-E meets the safety standards established by FFDCA, as amended by FQPA."[4] This approach is directly contrary to FDA's long-held view that these uses do not leave residues of concern on food contact surfaces and therefore do not require a dietary risk assessment. Before imposing any such requirement, EPA should engage in a process and explain why it rejects the FDA approach (and why it has not developed a harmonized approach with FDA) and allow public input on whether EPA's residue concerns are reasonable.

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[2] *See* Case 5026, Busan 1024 Registration Review Final Work Plan, December 14, 2007; and Case 5027, Oxazolidine-E Registration Review Final Work Plan, September 17, 2008.

[3] *See* Case 3053, Nuosept 145 Registration Review Final Work Plan, September 10, 2008.

[4] Oxazolidine-E Registration Review Final Work Plan, December 17, 2008, Docket No. EPA-HQ-OPP-2008-0404 at [HYPERLINK "http://www.regulations.gov"].

The Panel has sought but not found any information on what constitutes a "Tier 1 dietary screening level assessment" and does not refer to any documented process that the Panel can find. This is particularly a concern in situations such as this where EPA requires a dietary assessment for an active ingredient without food uses. Also, EPA has offered no explanation of its authority to require an FQPA risk assessment in this situation.

Example 2: Assumption that All Silver Products are Nanoscale

When EPA began to address marketing claims for "nano" products containing silver, the guidance and approaches were fluid and unclear. EPA placed the burden on registrants to demonstrate that products containing silver are not nano scale, often by generating successive studies to answer multiple, evolving questions from a reviewer. The problem was exacerbated by the lack of any consistency of what is considered to be nanotechnology. Certain registrants were required to spend significant amounts of money and time to refute EPA assumptions.

Example 3: Dermal Sensitization

Through its Isothiazolone Task Force (IT Task Force), the Panel has become aware of the Antimicrobial Division's (AD) effort to develop a new approach to testing and evaluating dermal sensitizers.[5] While we have not been provided with any documentation of the reason for this initiative by EPA, EPA representatives have informed the IT Task Force that the effort stems from Agency reviewers seeing internet-based information linking material preservatives to skin sensitization. Significantly, EPA did not cite peer-reviewed studies that meet EPA's statutory and regulatory obligations for transparency and data quality. As a result of this "curiosity," AD has been seeking restrictions on a family of active ingredients and seeking to have registrants develop an entirely new means of assessing dermal sensitization. We also are aware that through its efforts with the Interagency Center for the Evaluation of Alternative Toxicological Methods (ICCVAM), the Agency has been investigating alternative methods to assess sensitization. As this is an ongoing effort by the Agency, additional data from registrants should not have been required.

Example 4. Material Preservatives in Paint

Without prior notice to registrants of material preservatives used in paints, EPA began assessing those uses with an exposure model that had not previously been identified or discussed publicly. The "two hand immersion in a paint can" assessment approach was first noted during the reregistration of Octhilinone (OIT).[6] That assessment approach, which uses greatly oversimplified information and includes unsubstantiated assumptions, resulted in registrants having to provide data in an attempt to provide a more meaningful assessment approach and to support continued registration of those uses. In addition, registrants spent a significant time and

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[5] EPA called-in elicitation data under the Data Call-In for (2,6-dimethyl-1,3-dioxan-4-yl) acetate (Dimethoxane); GDCI-001001-1661. The EPA request requires human testing to sensitize individuals, which the Institutional Review Board (IRB), relied upon by some registrants, will not approve.

[6] *See* EPA-HQ-OPP-2007-0414 at www. regulations.gov.

effort to provide scientifically based explanations in an attempt to refute the Agency's assumptions. This is an example of where the Agency has decided to use an unproven approach to risk assessment without taking into account scientific considerations or public input, resulting in registrants having to provide data and other supporting information to overcome those deficiencies.